REMARKS

Status of the Claims

Claims 1-5 and 14-35 are pending, with claims 1, 2, 16, 18, and 20-23 being independent. Claims 6, 36, and 37 have been canceled herein without prejudice to or disclaimer of the subject matter contained therein as drawn to non-elected subject matter pursuant to the restriction requirement. Without conceding the propriety of the rejections, claims 1- 5, 14-16, 18, 20-26, and 30-35 have been amended and claims 17 and 19 have been canceled to even more clearly recite and distinctly claim particularly preferred embodiments of the present invention. Applicants expressly reserve the right to file one or more continuation and/or divisional applications directed to any subject matter canceled herein. Support for the amendments may be found throughout the specification, including, in the original claims and at page 13, line 32 – page 14, line 31. Therefore, no new matter has been added herein.

Initially, Applicants would like to thank the Examiner for conducting an interview with Applicants' representatives on October 6, 2005, to discuss the outstanding rejections. Applicants appreciate the Examiner's recognition that the rejection of §102(b) should be a rejection under §103, as provided in the Interview Summary. Also discussed were the unexpected properties of (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl] sulfonyl]imidazol[4,5-b]pyridine. In this regard, Applicants submit herewith a declaration of George Sachs, M.D., D.Sc., pursuant to 35 U.S.C. § 1.132 regarding these properties.

Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections in view of the foregoing amendments, the attached declaration pursuant to 35 U.S.C. § 1.132, and the following remarks.

Applicants note that, as discussed during the interview, if any outstanding issues remain after submission of the present response, Applicants would appreciate a telephone call from the Examiner so that such issues may be resolved expeditiously. Furthermore with regard to expediting prosecution, Applicants note that a ***Petition to Make Special*** was filed on March 22, 2005 and granted.

Restriction Requirement

With regard to the restriction requirement presented telephonically, Applicants confirm election of Group 1, claims 1-5 and 14-35, drawn to tenatoprazole compounds (*i.e.*, (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfonyl]imidazol[4,5-b]pyridine compounds), compositions, and methods of use. In order to expedite prosecution of the present application, claims 6, 36, and 37 have been canceled herein without prejudice to or disclaimer of the subject matter contained therein as drawn to non-elected subject matter pursuant to the restriction requirement. Applicants expressly reserve the right to file one or more continuation and/or divisional applications directed to the non-elected subject matter canceled herein.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-5 and 14-35 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. It is asserted that the claims do not "adequately describe the nexus between the modulation of the protein pump receptor and a useful treatment of a digestive disease/conditions, other than ulcers".

Without conceding the propriety of the rejection, claims 16 and 18 have been amended herein in order to expedite prosecution of the present application. Specifically, claims 16 and 18 have been amended to recite the digestive disease/conditions recited in original claims 17 and 19, respectively, (*i.e.*, Barrett's syndrome (also known as "Barrett's oesophagus"), Zollinger-Ellison syndrome, and atypical and oesophageal symptoms of gastro-oesophageal reflux) and claims 17 and 19 have been canceled. Applicants respectfully submit that that a nexus between the proton pump receptor and the treatment of these named conditions does. Such a nexus is shown by the specification as-filed, as well as by what was known in the art at the time the present application was filed.

As stated in the present specification on page 1, lines 5-14, 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl]imidazo[4,5-b]pyridine (hereinafter "tenatoprazole") belongs to the class of drugs known as proton pump inhibitors (PPIs). PPIs inhibit the secretion of gastric acid. Therefore, PPIs may be used to treat dyspepsia, peptic ulcers (PUD), Zollinger-Ellison syndrome, gastroesophageal reflux disease, (GORD/GERD), prevention of stress gastritis, gastrinomas, and other digestive acid-related conditions.

PPIs were well known in the art at the time the present application was filed for the treatment of digestive acid-related conditions, including those recited by the presently amended claims. As set forth in Goodman & Gilman's The Pharmacological *Basis of Therapeutics* (10th Edition, Hardman et al. ed., (2001) New York: McGraw-Hill Medical Publishing Division, page 1007), PPIs enter the parietal cells by way of the blood, and accumulate. They are activated by a proton-catalyzed process that results in the formation of sulfenamids or sulfenic acid, which binds to cysteines from H+, K+, and/or ATPase. Thus, PPIs can greatly reduce the production of acid.

Page 1009 of *Goodman & Gilman's The Pharmacological Basis of Therapeutics* notes that PPIs may be used to promote the healing of ulcers, to treat gastric esophageal reflux disease (GERD), and to treat Zollinger-Ellison syndrome. Figure 37-6 on page 1015 provides that PPIs are indicated for the treatment of GERD with esophagitis, and in the case of chronic and unrelenting symptoms, including Barrett's metaplasia and stricture.

Harrison's Principles of Internal Medicine (13th Edition, Isselbacher et al. ed., (1994) New York: McGraw-Hill, Inc., pages 1375-77) describes Zollinger-Ellison syndrome and state that it may be treated with parietal cell H+, K+, ATPase inhibitors.

For the Examiner's convenience copies of the relevant portions of these documents are attached.

Therefore, Applicants submit that the specification, in combination with what was known in the art at the time the present application was filed, provides a nexus between the presently claimed digestive conditions and PPIs, specifically (-) tenatoprazole.

Claims 1-5 and 14-35 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. It is asserted that undue experimentation would be required to show a nexus between the proton pump receptor and the treatment of digestive disease other than ulcers. Applicants respectfully traverse.

As stated in *Ex parte Forman* (230 USPQ 546 1986) the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims.

As, the Office is aware, "[a] patent need not teach, and preferably omits, what is well known in the art." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Thus, not every last detail is to be described, else patent specifications would turn into production specifications, which they were never intended to be. *Staehelin v. Secher*, 24 U.S.P.Q.2d 1513, 1516 (Bd. Pat. App. & Int. 1992). Applicants submit that the specification, combined with what is known in the art, provides adequate description of how to make and use (-) tenatoprazole for the treatment of the presently claimed digestive conditions.

As described above, claims 16 and 18 have been amended herein in order to expedite prosecution of the present application. Specifically, claims 16 and 18 have been amended to recite the digestive disease/conditions recited in original claims 17 and 19, respectively, (*i.e.*, Barrett's syndrome, Zollinger-Ellison syndrome, and atypical and oesophageal symptoms of gastro-oesophageal reflux) and claims 17 and 19 have been canceled. Also as discussed above, a nexus between PPIs and the treatment of these claimed conditions does exist, and would be apparent to the skilled artisan at the time the application was filed.

Applicants submit that the amount of direction or guidance presented and the nature of the invention are such that undue experimentation would not be required to practice the claimed methods of treatment. The state of the art is such that the relationship between proton pump receptors (and the inhibition of proton pumps by PPIs) and diseases and conditions caused/related to hypersecretion of acids was well known at the time of filing. As set forth above, *Goodman & Gilman's The Pharmacological Basis of Therapeutics* and *Harrison's Principles of Internal Medicine* describe the functionality of PPIs, as well as acid-related conditions and their symptoms, which may be readily treated and relieved by PPIs. Thus, the state of the prior art and relative skill of those in the relevant art were such that undue experimentation would not be required to practice the present methods.

With regard to the scope of the presently amended claims, the breadth of the claims is commensurate with specific digestive conditions/diseases, all relating to gastric acid.

Applicants submit that the requirements for enablement, as set forth in *Forman*, have been satisfied. As such, the skilled artisan would not require undue experimentation to practice the present methods.

For at least the above reasons, Applicants request that the rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-5 and 14-35 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite due to recitation of "tenatoprazole". Without conceding the propriety of the rejection, claims 1- 5, 14-16, 18, 20-26, and 30-35 have been amended to recite formal chemical name for tenatoprazole, namely, (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfonyl]imidazol[4,5-b]pyridine, in order to expedite prosecution. Accordingly, Applicants respectfully submit that this rejection has been obviated and respectfully request withdrawal thereof.

Rejections under 35 U.S.C. § 102(b)

Claims 1-5 and 14-35 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kakinoki (CA 131:208915) and Uchiyama (CA 131:139269 and CA 131:125259).

As stated in the Office Action, Kakinoki and Uchiyama disclose the racemic mixture of tenatoprazole, (*i.e.*, (±)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfonyl]imidazol[4,5-b]pyridine).

Applicants respectfully submit that disclosure of a racemate or racemic mixture makes ***prima facie obvious*** the separate enantiomers of the racemate; however, such disclosure does ***not*** anticipate the separate enantiomers. See *Brenner et al. v. LADD, Comr. Pats.*, 147 USPQ 87 (D.C. D.C. 1965) stating that "in the absence of unexpected or unobvious beneficial properties, an optically active isomer is unpatentable over either the isomer of opposite rotation or, as in this case, the racemic compound itself."; *In re Adamson et al.*, 275 F.2d 952, 125 USPQ 233 (CCPA 1960); *Sterling Drug Inc. v. Watson*, 135 F.Supp. 173, 108 USPQ 37 (D.C. D.C. 1955); *Emory University v. Glaxo Wellcome Inc.*, 44 USPQ2d 1407 (D.C. N.Ga.); *In re May*, 574 F.2d 1082, 197 USPQ 601 (CCPA 1960), and *In re Anthony*, 162 USPQ 594 (CCPA 1969). Accordingly, Applicants respectfully submit that the rejection raised in the Office Action should have been one of *prima facie* obviousness in view of Kakinoki and Uchiyama, and as provided above, Applicants appreciate the Examiner's recognition that the proper rejection was under 35 U.S.C. § 103, as provided in the Interview Summary.

In response to a rejection of *prima facie* obviousness, as discussed during the interview, Applicants respectfully submit that the (-) enantiomer evidences unexpected and

unobvious beneficial properties in view of both the racemic compound and the (+) enantiomer. In this regard, Applicants submit herewith a declaration of George Sachs, M.D., D.Sc., pursuant to 35 U.S.C. § 1.132 regarding these unexpected and unobvious beneficial properties. In view thereof, Applicants respectfully submit that for at least these reasons, the (-) enantiomer is non-obvious over the disclosure of the racemate, and Applicants respectfully request that the outstanding rejection under 35 U.S.C. § 102(b) be withdrawn.

Conclusion

Without conceding the propriety of the rejections, the claims have been amended, as provided above, to even more clearly recite and distinctly claim Applicants' invention and to pursue an early allowance. For the reasons noted above, the art of record does not disclose or suggest the inventive concept of the present invention as defined by the claims.

In view of the foregoing amendment, remarks, and the attached declaration of George Sachs, M.D., D.Sc., pursuant to 35 U.S.C. § 1.132, reconsideration of the claims and allowance of the subject application is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited. Furthermore with regard to expediting prosecution, Applicants note that a Petition to Make Special was filed on March 22, 2005 and granted.

Respectfully submitted,
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